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(21) International Application Number: PCT/NL97/00615 (22) International Filing Date: 10 November 1997 (10.11.97) (30) Priority Data: 1004488 11 November 1996 (11.11.96) NL (71) Applicant (for all designated States except US): MINOTARA CORPORATION N.V. [NL/NL]; Pietermaai 15, Curaçao (AN). (72) Inventor; and (75) Inventor/Applicant (for US only): KANTERS, Adrianus, Wilhelmus, Johannes [NL/NL]; Middena#kerweg 1, NL-5741 HS Beck en Donk (NL). (74) Agents: VAN KAN, J., J., H. et al.; ALGEMEEN OCTROOIBUREAU, World Trade Center, Past. Petersstraat 160, NL-5612 LV Eindhoven (NL).		(81) Designated States: AL, AM, AT, AT (Utility model), AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ (Utility model), DE, DE (Utility model), DK, DK (Utility model), EE, EE (Utility model), ES, FI, FI (Utility model), GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK (Utility model), SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i> <i>In English translation (filed in Dutch).</i>
(54) Title: AQUEOUS NUTRITIVE PREPARATION COMPRISING LACTIC ACID, ORGANIC ACID AND CHELATED TRACE ELEMENTS (57) Abstract <p>The invention relates to an aqueous nutritive preparation substantially with a base of lactic acid and/or derivatives thereof and one or more other organic acids and trace elements, wherein the elements selected from the group consisting of copper, zinc, phosphorus, manganese, magnesium, iodine, selenium and cobalt are present in a chelate bonding in an amount of 0.01 – 25 per cent by weight. The invention furthermore relates to methods for preparing such a nutritive preparation, as well as to the use of such a nutritive preparation in drinking water or in wet feed and to the use of said nutritive preparation for treating hooves of animals.</p>		

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AQUEOUS NUTRITIVE PREPARATION COMPRISING LACTIC ACID, ORGANIC ACID AND CHELATED TRACE ELEMENTS

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The present invention relates to an aqueous nutritive preparation substantially with a base of lactic acid and/or derivatives thereof and one or more organic acids and trace elements, to methods for preparing such a nutritive preparation, to the use of such a nutritive preparation in drinking water or in wet feed in intensive stock farming and to the drinking water or the wet feed thus obtained. The present invention furthermore relates to the use of an aqueous nutritive preparation for treating hooves of animals.

15 A aqueous nutritive preparation of this kind, which is used as an anti-microbial composition for inhibiting the growth of detrimental microbes, is known from international patent application WO 96/24248. The anti-microbial component comprises 50 - 99.8% per cent by weight of a substituted or non-substituted C_1 - C_4 -monocarboxylic acid, and about 0.2 - 30 per cent by weight of the ester of a substituted or non-substituted benzoic acid. Formic acid, acetic acid, propionic acid, lactic acid and pyruvic acid are mentioned as suitable organic monocarboxylic acids. In addition to that the composition may contain certain salts of magnesium, zinc and copper, depending on its use.

25 British patent specification No. 1 048 724 relates to a feed supplement for ruminants, which feed supplement comprises a non-toxic hydroxy organic compound selected from lactic acid, a metal salt thereof or a monohydric alcohol, excluding ethanol, or a di, tri or higher polyhydric alcohol, and a synthetic source of nitrogen.

30 The use of lactic acid in an aqueous nutritive preparation to be used in animal feed is also known from British patent applications Nos. 2 001 233 and 2 055 034.

35 Japanese patent application JP 53 111 010 A relates to a stable sorbic acid suspension for use in improving the storage properties of drinks and foodstuffs. Besides sorbic acid the suspension may also contain lactic acid, citric acid and malic acid, for example.

European patent application No. 0 701 778 relates to a method for preserving foodstuffs and to the foodstuffs thus obtained, whereby such foodstuffs are mixed with an aqueous potassium sorbate solution and an aqueous solution of an acid, for example phosphoric acid, lactic acid or sulphuric acid by using an intensive admixing process.

A aqueous nutritive preparation which is used as a disinfectant for drinking water, for example, is also known from European patent application No. 0 711 253. Benzoic acid, sorbic acid, propionic acid, formic acid, citric acid, tartaric acid, lactic acid, malic acid, acetic acid, ascorbic acid, hydrochloric acid, sulphuric acid, and also the salts, derivates and ester compounds and mixtures are mentioned as suitable agents for effecting a reduction of the germination index and stabilising drinking water. A preferred agent consists of 0.1 - 10 g of sodium benzoate and 0.1 - 10 g of sorbic acid per litre of water.

The above-described, prior art aqueous nutritive preparations with a base of lactic acid and/or derivates thereof and one or more other organic acids and trace elements have as a drawback that the free trace elements will precipitate during storage. As soon as a trace element precipitates in the aqueous nutritive preparation, the element as such is no longer biologically active, as a result of which an important function of the trace element is lost, namely its advantageous influence on the progress of the enzymatic reaction. Moreover, with the prior art aqueous nutritive preparations with a base of lactic acid it is necessary to adjust a critical pH value in order to prevent precipitation. This has led to certain restrictions with regard to the freedom to select acids to be added to the nutritive preparation.

The object of the present invention is therefore to provide an aqueous nutritive preparation substantially with a base of lactic acid and/or derivates thereof and one or more other organic acids and trace elements, which nutritive preparation obviates the above-described drawbacks. In addition to that it is desirable to provide an aqueous nutritive preparation which can be added in small amounts to drinking water or to wet feed in order to suppress the growth of fungi, yeasts, salmonella bacteria, streptococci, staphylococci, coli, pseudomonas and other pathogens.

The present invention as referred to in the introduction is characterized in that one or more trace elements selected from the group

consisting of copper, zinc, phosphorus, manganese, magnesium, iodine, selenium and cobalt are present in a chelate bonding in an amount of 0.01 - 25 per cent by weight in said aqueous nutritive preparation. If this amount is more than 25 per cent by weight, the trace elements will no longer be soluble in water, as a result of which precipitation of the essential trace elements will occur as yet. With amounts smaller than 0.01 per cent by weight it is no longer possible to observe an advantageous effect of the addition of the trace elements in the chelate bonding. The fact that the trace elements are present in a chelate bonding leads to an enhanced stability of the trace elements in the final aqueous nutritive preparation in comparison with the aqueous nutritive preparations known from the prior art, in which nutritive preparations the trace elements are present in the salt form.

The term chelate is to understood to mean a compound which comprises at least two "attaching points", which attaching points are oriented such that hexagonal or pentagonal ring structures can be formed. The chelate-forming agents are indicated by the number of attaching points, thus bidentates (two attaching points), tridentates (three attaching points), quadridentates, pentadentates, hexadentates and the like can be distinguished. A trace element may also have been chelated by using several chelating agents, however. Since the attaching points bind the trace element, the chelating agent enhances the stability of the trace element. The strong bond between the trace element and the chelating agents results in chelate bondings which comprise improved chemical properties in comparison with the free trace elements, in particular as regards the prevention of precipitation at a critical pH value.

According to the present invention the term derivates is understood to mean lactic acid compounds derived from lactic acid, that is salts, ester compounds, and also mixtures thereof. The amount of lactic acid and/or derivates thereof is preferably 1 - 85 per cent by weight, if this amount is less than 1 per cent by weight, its effect as regards the inhibition of bacterial growth will be insufficient. If the amount is more than 85 per cent by weight, the nutritive preparation obtained will exhibit an unpleasant odour. In addition to that the viscosity of the agent will be high, as a result of which its processing will be problematic.

Research has shown that the addition of lactic acid to drinking water prevents the growth of fungi, yeasts, salmonella bacteria, streptococci, staphylococci, coli, pseudo-monas and other pathogens. In addition to that, lactic acid has appeared to be a highly suitable carrier for preserving a liquid mixture of minerals, vitamins, amino acids and the like. Furthermore it has become apparent that lactic acid has a very favourable influence on the gastro-intestinal tract of animals. The fact is that the addition of lactic acid to drinking water in intensive stock forming has not caused diarrhea with the animals, whilst the addition of sulphuric acid, for example, has caused serious problems. Lactic acid obtained by fermentation of lactic acid bacteria is a natural product, which provides an optimum intestinal flora, in particular in the small intestine. Another remarkable aspect is that lactic acid has a positive influence on the excretion of phosphate and nitrogen compounds by animals. A decreased excretion of these compounds benefits the environment.

The aqueous nutritive preparation according to the present invention is furthermore characterized in that it contains 0.5 - 25 per cent by weight of oligosaccharides. According to the present invention oligosaccharides comprise hydrocarbons having 2 - 10 sugar units. Most oligosaccharides are soluble in water and are decomposed therein by the body's own intestinal enzymes; their selectivity consists of stimulating the growth of certain populations within the microbial ecosystem in the intestine. Moreover, there are indications that said oligosaccharides can prevent pathogens and enterotoxins adhering to the wall of the intestine.

Although a drinkable preparation for animals, which serves to preserve their good health, is known from Japanese patent application JP 72 28 533, which preparation contains calcium lactate, sucrose, malic acid, thiamine hydrochloride, taurine and caffeine, it is not known from the said publication to use oligosaccharides in combination with trace elements in the chelate bonding in an aqueous nutritive preparation with a base of lactic acid.

The addition of oligosaccharides will provide a nutritive preparation which contains all essential constituents for the animals. The use of oligosaccharides, which compounds are considered to be natural growth stimulants, furthermore obviates the use of synthetic

growth stimulants. Recent legislation in Scandinavia has banned the use of such synthetic substances in nutritive preparations for animals.

Furthermore the aqueous nutritive preparation preferably contains 1 - 19 per cent by weight of hydroxy acetic acid, 0.5 - 5 per cent by weight of citric acid, and 0.1 - 5 per cent by weight of sorbic acid. The use of other organic acids besides lactic acid has an advantageous effect on the occurrence of harmful micro-organisms in the drinking water or in wet feed. Furthermore, the addition of hydroxy acetic acid lessens the unpleasant odour produced by the lactic acid. The addition of citric acid and sorbic acid has a preserving effect on the aqueous nutritive preparation. Furthermore it has become apparent that when organic acids are added in a combination thereof the synergetic effect obtained is better than when only lactic acid and/or derivatives thereof are used.

Furthermore the nutritive preparation preferably contains 0.1 - 1.0 per cent by weight of isopropanol, 0.01 - 0.5 per cent by weight of quaternary ammonium chloride, 0.1 - 5 per cent by weight of dodecyl dimethyl ammonium chloride, 0.01 - 0.5 per cent by weight of polydimethyl siloxane. By adding minerals to the drinking water it is ensured that the nutritive preparation contains all the constituents that the animals need.

The present invention furthermore relates to a method for preparing the aqueous nutritive preparation, which method is characterized in that an aqueous mixture of lactic acid, hydroxy acetic acid and sorbic acid is admixed with an aqueous mixture of citric acid, hydroxy acetic acid, isopropanol, quaternary ammonium chloride, dodecyl dimethyl ammonium chloride and polydimethyl siloxane, after which oligosaccharides and trace elements are added to the solution thus obtained. If oligosaccharides are directly added to the aqueous mixture containing lactic acid, undesirable precipitation will occur. The admixing of the mixture containing lactic acid and the mixture containing citric acid is carried out at a temperature of for example 40 - 90 °C, preferably 60 - 80 °C. The advantage of such a method is that no premature precipitation will occur. Moreover, the shelf life of two separate mixtures will be longer in the embodiment wherein all the components are present in one mixture.

The aqueous nutritive preparation thus prepared is used in drinking water or in wet feed in intensive stock farming, preferably

in an amount of 0.5 - 3 litres of aqueous nutritive preparation per 1000 litres of drinking water or wet feed. If the amount of aqueous nutritive preparation is less than 0.5 litres per 1000 litres, the micro-organism-inhibiting effect will be too small, and if the amount is more than 3
5 litres per 1000 litres, no enhanced micro-organism-inhibiting effect will be observed. The addition of the aqueous nutritive preparation according to the present invention to dry feed preferably takes place by spraying the aqueous nutritive preparation onto the dry feed. Said spraying with the aqueous nutritive preparation furthermore has a preserving effect on
10 the dry feed.

The pH value of the drinking water or the wet feed after the addition of the aqueous nutritive preparation is preferably lower than 6, more preferably 3.5 - 4.5. If the pH value is higher than 6, the micro-organism-inhibiting effect that is observed will be insufficient.

15 The present invention furthermore relates to the use of the aqueous nutritive preparation according to the present invention for treating hooves of animals. A great many animal waste products, such as urine and manure, are present on the floor of a stable. Such harmful materials accumulate in the small openings in the hooves of animals. After
20 some time the hoof will become inflamed, which has an adverse effect on the animal's well-being. Surprisingly it has become apparent that if hooves of animals are treated with the aqueous nutritive preparation according to the present invention, hoof inflammation will be prevented in an advantageous manner. The aqueous nutritive preparation may be applied
25 directly to the hoof to be treated, but it is also possible to add the aqueous nutritive preparation to a bath, in which the animal to be treated is made to stand. Thus the aqueous nutritive preparation has a disinfecting effect on the hooves of animals.

The present invention will now be explained with
30 reference to the examples. It should be understood, however, that the present invention is by no means limited to such special embodiments. Although the examples relate to the administering of aqueous nutritive preparations to pigs and chickens, it should be understood that the present aqueous nutritive preparation can also be used for other animals, for
35 example cows, goats, sheep and the like.

Example 1

An aqueous solution (A) of lactic acid was prepared

by dissolving 70 g of liquid lactic acid, 10 g of liquid hydroxy acetic acid and 0.3 g of powdery sorbic acid in 29.7 g of water. The solution (A) thus obtained was thoroughly stirred and a clear solution was obtained. Then 12 g of the trace elements copper, zinc, phosphorus and cobalt present in the chelate bonding were added to the clear solution. The aqueous nutritive preparation (F) thus obtained was added to the drinking water for salmonella-infected chickens in an amount of 2 l per 1000 l of drinking water. After 2 days the gastro-intestinal tract of said chickens appeared to be free from salmonella.

10 Example 2

 An amount of 10 g of oligosaccharides was added to the aqueous nutritive preparation (F) prepared in example 1 at a temperature of 70 °C. The mixture (G) thus obtained was added to drinking water for salmonella-infected chickens in the same amounts as used in example 1. The use of oligosaccharides increased the uptake of the trace elements present in the chelate bonding into the gastro-intestinal tract. Further analysis of the excrements showed that the addition of oligosaccharides has resulted in an improved digestion of protein, because no undigested food remnants were found in the excrements.

20 Comparative example 1

 An aqueous solution (A) of lactic acid was prepared in a manner corresponding with example 1 by dissolving 70 g of liquid lactic acid, 10 g of liquid hydroxy acetic acid and 0.3 g of powdery sorbic acid in 29.7 g of water. The solution (A) thus obtained was thoroughly stirred and a clear solution was obtained. Then another water-containing solution (B) was prepared by adding the following compounds: 12.9 g of citric acid, 8.7 g of hydroxy acetic acid, 0.66 g of isopropanol, 0.02 g of quaternary ammonium chloride, 3.04 g of dodecyl dimethyl ammonium chloride and 0.08 g of polydimethyl siloxane to 49.2 g of water. After the above components had been added to the water while stirring, the clear solution (B) was obtained. The final aqueous nutritive preparation was obtained by combining 9 parts of solution (A) with 1 part of solution (B). The solution (C) thus obtained was added to the drinking water for salmonella-infected chickens in an amount of 2 l per 1000 l of drinking water. The drinking water was used for a period of 3 days. Then the amount of solution (C) was reduced from 2 l to 1 l per 1000 l of drinking water over a period of 4 days. After this period the gastro-intestinal tract

of said chickens appeared to be free from salmonella.

Comparative example 2

5 An amount of 10 g of oligosaccharides was added to the aqueous nutritive preparation (F) obtained in comparative example 1, whereby said mixing took place. The aqueous nutritive preparation (D) thus
10 obtained was added to wet feed for pigs in the same amounts as used in example 3. The use of oligosaccharides increased the uptake of the minerals into the gastro-intestinal tract. The same nutritive preparation (C) as prepared in example 1, not containing any oligo-saccharides in this case,
15 was added to wet feed for pigs. Analysis of the pig excrements showed that large portions of feed remained undigested. It is apparent that the addition of oligosaccharides results in an improved digestion of protein and is conducive to a favourable natural flora in the intestinal tract.

Example 3

15 An amount of 5 per cent by weight of the trace elements copper, zinc, phosphorus, manganese, magnesium, iodine, selenium and cobalt in a chelate bonding was added to the aqueous nutritive preparation (D) of comparative example 2. The addition of these special trace elements resulted in a balanced nutritive preparation (E) for chickens. In addition,
20 after a period of 2 - 3 days the salmonella-infected chickens were free from salmonella bacteria. The preparation was used in the amounts stated in example 1. When the aforesaid trace elements were not used in chelate form, it took as long as 7 days before the salmonella-infected chickens were declared free from salmonella.

25 Comparative example 3

An aqueous solution containing 50% lactic acid was prepared and fed to salmonella-infected chickens in an amount of 1.5 l per 1000 l of drinking water. After a period of 12 days the gastro-intestinal tract of the chickens appeared to be free from salmonella.

30 Example 4

The aqueous nutritive preparation of example 1 was added in an amount of 1.5 l per 1000 l of water. The composition thus obtained was transferred to a so-called walk-in trough for stables. The cows were led through this walk-in trough every day upon entering and leaving the
35 stable. The number of inflammations of the hooves decreased considerably in comparison with a control group of cows that were not treated with the aqueous nutritive preparation of example 1.

CLAIMS

1. An aqueous nutritive preparation substantially with a base of lactic acid and/or derivatives thereof and one or more other organic acids and trace elements, characterized in that one or more trace elements selected from the group consisting of copper, zinc, phosphorus, manganese, magnesium, iodine, selenium and cobalt are present in a chelate bonding in an amount of 0.01 - 25 per cent by weight.
2. An aqueous nutritive preparation according to claim 1, characterized in that said preparation contains 0.5 - 25 per cent by weight of oligosaccharides.
3. An aqueous nutritive preparation according to claims 1 - 2, characterized in that said preparation contains 0.1 - 1.0 per cent by weight of isopropanol.
4. An aqueous nutritive preparation according to claims 1 - 3, characterized in that said preparation contains 0.01 - 0.5 per cent by weight of quaternary ammonium chloride.
5. An aqueous nutritive preparation according to claims 1 - 4, characterized in that said preparation contains 0.1 - 5 per cent by weight of dodecyl dimethyl ammonium chloride.
6. An aqueous nutritive preparation according to claims 1 - 5, characterized in that said preparation contains 0.01 - 0.5 per cent by weight of polydimethyl siloxane.
7. An aqueous nutritive preparation according to claims 1 - 6, characterized in that said preparation contains 1 - 19 per cent by weight of hydroxy acetic acid.
8. An aqueous nutritive preparation according to claims 1 - 7, characterized in that said preparation contains 0.5 - 5 per cent by weight of citric acid.
9. An aqueous nutritive preparation according to claims 1 - 8, characterized in that said preparation contains 0.1 - 5 per cent by weight of sorbic acid.
10. A method for preparing an aqueous nutritive preparation according to claim 1, characterized in that an aqueous mixture of lactic acid and/or derivatives thereof and one or more other organic acids is prepared, after which one or more trace elements are added in the chelate bonding.

11. A method for preparing an aqueous nutritive preparation according to claims 2 - 9, characterized in that the oligosaccharides are added to the mixture containing lactic acid and/or derivatives and one or more other organic acids at a temperature of 40 - 90 °C, after which one or more trace elements in the chelate bonding are added to the composition thus formed.

12. A method for preparing an aqueous nutritive preparation according to claims 1 - 9, characterized in that an aqueous mixture of lactic acid, hydroxy acetic acid and sorbic acid is admixed with an aqueous mixture of citric acid, hydroxy acetic acid, isopropanol, quaternary ammonium chloride, dodecyl dimethyl ammonium chloride and polydimethyl siloxane, after which oligosaccharides and trace elements present in the chelate bonding are added to the solution thus obtained.

13. Use of the aqueous nutritive preparation according to any one of the claims 1 - 9 in drinking water or in wet feed in intensive stock farming, characterized in that 0.5 - 3 l of aqueous nutritive preparation are added per 1000 l of drinking water or wet feed.

14. Drinking water or wet feed obtained in accordance with claim 13, characterized in that the pH value is lower than 6.

15. Use of the aqueous nutritive preparation according to any one of the claims 1 - 9 for treating hooves of animals.

INTERNATIONAL SEARCH REPORT

International Application No.

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A CLASSIFICATION OF SUBJECT MATTER

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According to International Patent Classification (IPC) or to both national classification and IPC

B FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 A23K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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INTERNATIONAL SEARCH REPORT

Inter nal Application No

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication where appropriate of the relevant passages	Relevant to claim No
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